UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,915	04/27/2001	Paul David Robbins	AP32737-072396.0225	1483

21003 7590 08/26/2003

BAKER & BOTTS
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
GIBBS, TERRA C	

ART UNIT	PAPER NUMBER
1635	17

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,915	ROBBINS ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34,41-59 and 63-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *41 and 63* is/are allowed.

6)☐ Claim(s) *1, 2, 4-7, 9-15, 17-30, 32-34, 42-58, 64 and 65* is/are rejected.

7)☐ Claim(s) *3,8,16,31 and 59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a response to the Amendment filed June 6, 2003, in Paper No. 11.

Claims 35-40, 60-62, 66, and 67 have been canceled. Claims 1-7, 9, 11, 12, 15, 26, 41-44, 46, 47, and 49 have been amended.

Claims 1-34, 41-59, and 63-65 are pending in the instant application.

Claim Objections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 26 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. This rejection is withdrawn in view of Applicants Amendment, filed June 6, 2003, in Paper No. 11.

Claim Rejections - 35 USC § 101

Claims 1-6, 7-14, 41, 42 and 43-48 ~~are~~ were rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. This rejection is withdrawn in view of Applicants Amendment, filed June 6, 2003, in Paper No. 11.

KAL 08-25-03

Claim Rejections - 35 USC § 103

Claims 1-25, 27-34, 41-59 and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Storm et al. [U.S. Publication No. US2002/0164311 A1] in further view of

Thomson et al. [U.S. Patent No. 5,871,728] Lu et al$_1$. (Journal of Leukocyte Biology, 1999 Vol. 66:293-296) Lu et al$_2$. (Gene Therapy, 1999 Vol. 6:554-563) and Bielinska et al. (Science, 1990 Vol. 250:997-1000). This rejection is withdrawn in view of Applicants arguments, filed June 6, 2003, in Paper No. 11.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 12, 15, 17, 18, 19, 20, 26, 45, 47, 49, 50, 51, 52, 53, and 58, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite because claim 10 recites the term "cytokine" in line 1. There is insufficient antecedent basis for this limitation in the claim because claim 9, from which claim 10 depends, has the term "cytokines" which is plural. Correction is required.

Claim 12 is indefinite because claim 12 recites the term "said isolated tolerogenic dendritic cells" in line 2. There is insufficient antecedent basis for this limitation in the claim because claim 7, from which claim 12 depends, has the term "isolated tolerogenic dendritic cell" which is singular. Correction is required.

Claim 15 is indefinite because claim 15 recites the term "said isolated tolerogenic dendritic cells" in lines 6 and 7. There is insufficient antecedent basis for this limitation in the

claim because claim 15 only refers to "isolated dendritic cells", not "isolated tolerogenic dendritic cells". Correction is required.

Claims 17 and 19 are indefinite because claims 17 and 19 recite the term "said dendritic cells" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claims because claim 15, from which claims 17 and 19 depend, has the term "isolated dendritic cells". Correction is required.

Claim 18 is indefinite because claim 18 recites the term "cytokine" in line 1. There is insufficient antecedent basis for this limitation in the claim because claim 17, from which claim 18 depends, has the term "cytokines" which is plural. Correction is required.

Claim 20 is indefinite because claim 20 recites the term "said tolerogenic dendritic cells" in line 2. There is insufficient antecedent basis for this limitation in the claim because claim 15, from which claim 20 depends, has the term "isolated tolerogenic dendritic cells". Correction is required.

Claim 26 is indefinite because claim 26 recites the term "tolerogenic dendritic cells" in line 2. There is insufficient antecedent basis for this limitation in the claim because claim 15, from which claim 26 depends, has the term "isolated tolerogenic dendritic cells". Correction is required.

Claim 45 is indefinite because claim 45 recites the term "cytokine" in line 2. There is insufficient antecedent basis for this limitation in the claim because claim 44, from which claim 45 depends, has the term "cytokines" which is plural. Correction is required.

Claim 47 is indefinite because claim 47 recites the term "said isolated tolerogenic dendritic cells" in line 2. There is insufficient antecedent basis for this limitation in the claim

because claim 43, from which claim 47 depends, has the term "isolated tolerogenic dendritic cell" which is singular. Correction is required.

Claim 49 is indefinite because claim 49 recites the term "said tolerogenic isolated dendritic cells" in line 7. There is insufficient antecedent basis for this limitation in the claim because claim 49 only refers to "isolated dendritic cells", not "isolated tolerogenic dendritic cells". Correction is required.

Claims 50 and 52 are indefinite because claims 50 and 52 recite the term "said dendritic cells" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claims because claim 49, from which claims 50 and 52 depend, has the term "isolated dendritic cells". Correction is required.

Claim 51 is indefinite because claim 51 recites the term "cytokine" in line 1. There is insufficient antecedent basis for this limitation in the claim because claim 50, from which claim 51 depends, has the term "cytokines" which is plural. Correction is required.

Claim 53 is indefinite because claim 53 recites the term "said dendritic cells" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claims because claim 49, from which claim 53 depends, has the term "isolated dendritic cells". Correction is required.

Claim 58 is indefinite because claim 58 recites the term "tolerogenic dendritic cells" in line 1. There is insufficient antecedent basis for this limitation in the claim because claim 49, from which claim 58 depends, has the term "tolerogenic isolated dendritic cells". Correction is required.

Claims 7, 9, 11, 15, 17, 19, 43, 44, 45, 46, 49, 50, and 52 are rejected under 35 U.S.C.

112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite because clam 7 recites the term "culturing said isolated dendritic cells" in line 6. It is unclear whether the cultured isolated dendritic cells of (c) are the immature isolated dendritic cells of (a) or the isolated dendritic cells incubated with an oligodeoxyribonucleotide of (b). Correction is required.

Claims 9 and 11 are indefinite because claims 9 and 11 recite the term "incubating the isolated dendritic cells" in lines 1-2. It is unclear whether the isolated incubated dendritic cells are the immature isolated dendritic cells of (a), the isolated dendritic cells incubated with an oligodeoxyribonucleotide of (b), or the cultured isolated dendritic cells of (c). Correction is required.

Claim 15 is indefinite because clam 15 recites the term "culturing said isolated dendritic cells" in line 6. It is unclear whether the cultured isolated dendritic cells of (c) are the immature isolated dendritic cells of (a) or the isolated dendritic cells incubated with an oligodeoxyribonucleotide of (b). Correction is required.

Claims 17 and 19 are indefinite because claims 17 and 19 recite the term "incubating the isolated dendritic cells" in lines 1-2. It is unclear whether the incubated isolated dendritic cells are the immature isolated dendritic cells of (a), the isolated dendritic cells incubated with an oligodeoxyribonucleotide of (b), or the cultured isolated dendritic cells of (c). Correction is required.

Claim 43 is indefinite because clam 43 recites the term "culturing said isolated dendritic cells" in line 6. It is unclear whether the cultured isolated dendritic cells of (c) are the immature

isolated dendritic cells of (a) or the isolated dendritic cells incubated with an oligodeoxyribonucleotide of (b). Correction is required.

Claims 44 and 46 are indefinite because claims 44 and 46 recite the term "incubating the isolated dendritic cells" in lines 1-2. It is unclear whether the incubated isolated dendritic cells are the immature isolated dendritic cells of (a), the isolated dendritic cells incubated with an oligodeoxyribonucleotide of (b), or the cultured isolated dendritic cells of (c). Correction is required.

Claim 45 is indefinite because claim 45 recites the term "cytokine" in line 1. There is insufficient antecedent basis for this limitation in the claim because claim 44, from which claim 45 depends, has the term "cytokines" which is plural. Correction is required.

Claim 49 is indefinite because clam 49 recites the term "culturing said isolated dendritic cells" in lines 6 and 7. It is unclear whether the cultured isolated dendritic cells of (c) are the immature isolated dendritic cells of (a) or the isolated dendritic cells incubated with an oligodeoxyribonucleotide of (b). Correction is required.

Claims 50 and 52 are indefinite because claims 50 and 52 recite the term "incubating the isolated dendritic cells" in lines 1-2. It is unclear whether the incubated isolated dendritic cells are the immature isolated dendritic cells of (a), the isolated dendritic cells incubated with an oligodeoxyribonucleotide of (b), or the cultured isolated dendritic cells of (c). Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-7, 9-15, 17-30, 32-34, 42, 47, 48, 53, 54, 64, and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is for lack of written description.

Claims 1, 2, 4-7, 9-15, 17-30, 32-34, 42, 47, 48, 53, 54, 64, and 65 are drawn to an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, or TGF-β; a method of producing said isolated tolerogenic dendritic cell; a method of using said isolated tolerogenic dendritic cell to enhance tolerogenicity, and a kit for enhancing tolerogenicity comprising said isolated tolerogenic dendritic cell.

The claimed invention encompasses an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising any viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, or TGF-β. The specification as filed provides only a description of an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of GM-CSF.

The specification provides only an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of GM-CSF. However, the specification as filed, does not provide sufficient description that would allow one of skill in the art to use SEQ ID NO. 1 to predict the structures of all oligodeoxyribonucleotides having one or more NF-κB binding sites; an adenoviral vector encoding CTLA4Ig to predict the structures of all viral vectors; and GM-CSF to predict the structures of all cytokines, as contemplated by the instant specification.

The specification fails to describe the complete structure of a representative number of species of the claimed genus. See the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement (Vol. 66, No. 4, pages 1099-1111). These guidelines state that: "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention." In the instant case, the

specification does not describe or identify characteristics that can be used to distinguish species of the claimed genus.

Additionally, "[T]he skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence."

Applicant's specification does not provide a sufficient number of representative species of an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, and further comprising any viral vector which would allow one of skill in the art to predict the structures of all members of the claimed genus of compounds. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Therefore, the specification does not describe the claimed compounds in such full and concise terms so as to indicate that the applicant had possession of these compounds at the time of filing of this application. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.).

Claims 1, 2, 4-6, and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, and further comprising an adenoviral vector encoding CTLA4Ig, does not reasonably provide enablement for an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 2, 4-6, and 42 are drawn to an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising any viral vector.

The instant invention specification provides methodologies for inhibiting NF-κB binding activity and allostimulatory function in bone marrow-derived dendritic cells using SEQ ID NO: 1 and incubating the cells in the presence of GM-CSF (see Figures 5 and 6, respectively). The instant invention specification also provides methodologies for prolonging heart allograft survival using bone marrow-derived dendritic cells pre-treated with SEQ ID NO: 1 (see Figure 8) and transfected with adenovirus encoding CTLA4Ig (see Table 1).

The specification does not provide particular guidance or particular direction for an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising any viral vector (see 35 U.S.C. 112, first paragraph rejection against claims 1, 2, 4-7, 9-15, 17-30, 32-34, 42, 47, 48, 53, 54, 64, and 65 for written description above).

The description does not provide particular guidance or particular direction for an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising any viral vector and therefore, one of ordinary skill in the art at the time of the invention would have required an undue amount of experimentation to make and use the claimed invention commensurate with the full scope of the claims. Due to the lack of specific guidance in the specification as filed and the lack of correlation between an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, and further comprising an adenoviral vector encoding CTLA4Ig; and an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising any viral vector, one of skill in the art would have to engage in trial and error experimentation to practice the claimed invention over the scope claimed. The quantity of experimentation required to practice the invention over the scope claimed would include the de novo determination of developing an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising any viral vector, where only an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, and further comprising an adenoviral vector encoding CTLA4Ig is taught.

Claims 7, 9-14, 44, 46, 47, and 48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is

SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of GM-CSF, does not reasonably provide enablement for a method of producing an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, or TGF-β. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 7, 9-14, 44, 46, 47, and 48 are drawn to a method of producing an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, or TGF-β.

The instant invention specification provides methodologies for inhibiting NF-κB binding activity and allostimulatory function in bone marrow-derived dendritic cells using SEQ ID NO: 1 and incubating the cells in the presence of GM-CSF (see Figures 5 and 6, respectively). The instant invention specification also provides methodologies for prolonging heart allograft survival using bone marrow-derived dendritic cells pre-treated with SEQ ID NO: 1 (see Figure 8) and transfected with adenovirus encoding CTLA4Ig (see Table 1).

The specification does not provide particular guidance or particular direction for a method of producing an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising any viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence

of one or more cytokines (see 35 U.S.C. 112, first paragraph rejection against claims 1, 2, 4-7, 9-15, 17-30, 32-34, 42, 47, 48, 53, 54, 64, and 65 for written description above).

The description does not provide particular guidance or particular direction for a method of producing an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, or TGF-β and therefore, one of ordinary skill in the art at the time of the invention would have required an undue amount of experimentation to make and use the claimed invention commensurate with the full scope of the claims. Due to the lack of specific guidance in the specification as filed and the lack of correlation between a method of producing an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of GM-CSF; and a method of producing an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, or TGF-β, one of skill in the art would have to engage in trial and error experimentation to practice the claimed invention over the scope claimed. The quantity of experimentation required to practice the invention over the scope claimed would include the de novo determination of developing a method of producing an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said

isolated tolerogenic dendritic cell in the presence of one or more cytokines, or TGF-β, where only a method of producing an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of GM-CSF is taught.

Claims 15, 17-29, 50, and 52-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of enhancing tolerogenicity in a mammalian transplant host, comprising the intravenous administration of an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of GM-CSF, does not reasonably provide enablement for a method of enhancing tolerogenicity in a mammalian host with an inflammatory related disease or arthritis, comprising any route of administration of an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, TGF-β, FK 506, or cyclosporine A. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 15, 17-29, 50, and 52-57 are drawn to a method of enhancing tolerogenicity in a mammalian host with an inflammatory related disease or arthritis, comprising any route of

administration of an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, TGF-β, FK 506, or cyclosporine A.

The instant invention specification provides methodologies for inhibiting NF-κB binding activity and allostimulatory function in bone marrow-derived dendritic cells using SEQ ID NO: 1 and incubating the cells in the presence of GM-CSF (see Figures 5 and 6, respectively). The instant invention specification also provides methodologies for prolonging heart allograft survival using bone marrow-derived dendritic cells pre-treated with SEQ ID NO: 1 (see Figure 8) and transfected with adenovirus encoding CTLA4Ig (see Table 1).

The specification does not provide particular guidance or particular direction for a method of enhancing tolerogenicity in a mammalian host with an inflammatory related disease or arthritis, comprising any route of administration of an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising any viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines (see 35 U.S.C. 112, first paragraph rejection against claims 1, 2, 4-7, 9-15, 17-30, 32-34, 42, 47, 48, 53, 54, 64, and 65 for written description above).

The description does not provide particular guidance or particular direction for a method of enhancing tolerogenicity in a mammalian host with an inflammatory related disease or arthritis, comprising any route of administration of an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic

cell in the presence of one or more cytokines, TGF-β, FK 506, or cyclosporine A, and therefore, one of ordinary skill in the art at the time of the invention would have required an undue amount of experimentation to make and use the claimed invention commensurate with the full scope of the claims. Due to the lack of specific guidance in the specification as filed and the lack of correlation between a method of enhancing tolerogenicity in a mammalian transplant host, comprising the intravenous administration of an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of GM-CSF; and a method of enhancing tolerogenicity in a mammalian host with an inflammatory related disease or arthritis, comprising any route of administration of an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, TGF-β, FK 506, or cyclosporine A, one of skill in the art would have to engage in trial and error experimentation to practice the claimed invention over the scope claimed. The quantity of experimentation required to practice the invention over the scope claimed would include the de novo determination of developing a method of enhancing tolerogenicity in a mammalian host with an inflammatory related disease or arthritis, comprising any route of administration of an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of one or more cytokines, TGF-β, FK 506, or cyclosporine A, where only a method of enhancing

tolerogenicity in a mammalian transplant host, comprising the intravenous administration of an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig, and further comprising incubating said isolated tolerogenic dendritic cell in the presence of GM-CSF is taught.

Claims 30, 32-34, 64 and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a kit for enhancing tolerogenicity in a mammalian transplant host, comprising an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig, does not reasonably provide enablement for a kit for enhancing tolerogenicity in a mammalian host, comprising an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 30, 32-34, 64 and 65 are drawn to a kit for enhancing tolerogenicity in a mammalian host, comprising an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector.

The instant invention specification provides methodologies for inhibiting NF-κB binding activity and allostimulatory function in bone marrow-derived dendritic cells using SEQ ID NO: 1

and incubating the cells in the presence of GM-CSF (see Figures 5 and 6, respectively). The instant invention specification also provides methodologies for prolonging heart allograft survival using bone marrow-derived dendritic cells pre-treated with SEQ ID NO: 1 (see Figure 8) and transfected with adenovirus encoding CTLA4Ig (see Table 1).

The specification does not provide particular guidance or particular direction for a kit for enhancing tolerogenicity in a mammalian host, comprising an isolated tolerogenic dendritic cell comprising any oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising any viral vector (see 35 U.S.C. 112, first paragraph rejection against claims 1, 2, 4-7, 9-15, 17-30, 32-34, 42, 47, 48, 53, 54, 64, and 65 for written description above).

The description does not provide particular guidance or particular direction for a kit for enhancing tolerogenicity in a mammalian host, comprising an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, and therefore, one of ordinary skill in the art at the time of the invention would have required an undue amount of experimentation to make and use the claimed invention commensurate with the full scope of the claims. Due to the lack of specific guidance in the specification as filed and the lack of correlation between a kit for enhancing tolerogenicity in a mammalian transplant host, comprising an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig; and a kit for enhancing tolerogenicity in a mammalian host, comprising an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, one of skill in the art would have to engage in trial and error experimentation to practice

the claimed invention over the scope claimed. The quantity of experimentation required to practice the invention over the scope claimed would include the de novo determination of developing a kit for enhancing tolerogenicity in a mammalian host, comprising an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide having one or more NF-κB binding sites, further comprising a viral vector, where only a kit for enhancing tolerogenicity in a mammalian transplant host, comprising an isolated tolerogenic dendritic cell comprising an oligodeoxyribonucleotide, wherein the oligodeoxyribonucleotide is SEQ ID NO: 1, further comprising an adenoviral vector encoding CTLA4Ig is taught.

Allowable Subject Matter

Claims 3, 8, 16, 31, and 59 are objected to as being depend upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 41 and 63 are allowable.

The closest prior art of record is that of Thomson et al. [U.S. Patent No. 5,871,728] who teach a method of enhancing tolerance in a host mammal to an allogeneic donor graft comprising (a) isolating immature mammalian dendritic cells from a donor mammal; (b) culturing said immature mammalian dendritic cells in the presence of a cytokine (c) isolating said cultured dendritic cells and (d) administering said cultured dendritic cells to the host mammal to enhance tolerance to said donor graft. However, Thomson et al do not teach or suggest inhibiting NF-κB

transcriptional activity by incubating the dendritic cells with an oligodeoxyribonucleotide having at least one NF-κB binding site.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

tcg
August 20, 2003

Karen Lacourciere
KAREN LACOURCIERE
PATENT EXAMINER